

## ABSTRACT OF THE DISCLOSURE

Arginine-containing cysteine-modifying compounds useful for MALDI-MS analysis of proteins are provided. These compounds termed isotope-coded ionization enhancement reagents (ICIER) can provide ionization enhancement in MALDI-MS, relative quantitation, and additional database searching constraints at the same time without any extra sample manipulation. More specifically, ICIER increase the ionization efficiency of cysteine-containing peptides by attachment of a guanidino functional group. ICIER also increase the overall hydrophilicity of these peptides due to the hydrophilic nature of ICIER and thus increase the percentage of recovery of these peptides during sample handling and processing such as in-gel digestion or liquid chromatography. Finally, a combination of both light and heavy ICIER provides an accurate way to obtain relative quantitation of proteins by MALDI-MS and additional database searching constraints (number of cysteine residues in every single peptide peak) to increase the confidence of protein identification by peptide mass mapping.